Advancing Bioscience to Improve Human Health

The Laboratory leverages its capabilities in the physical and engineering sciences to conduct research of national importance in bioscience and biotechnology. In partnership with academia, industry, and government, Livermore began the bioscience research program in 1963, with a focus on understanding how ionizing radiation affects human health. The work led to the development of technologies that helped launch the Human Genome Project, and activities now range from research in genomics to counter-bioterrorism to health-care technologies.

Understanding the Human Genome and DNA

An important milestone was reached in 2000 when the DOE Joint Genome Institute (JGI), with researchers from Livermore, Berkeley, and Los Alamos national laboratories, completed a "working draft" sequence of human chromosomes 5, 16, and 19. The accomplishment is a major step—but only the first—toward understanding genetic material. In 2001, Livermore researchers improved the draft sequence and pursued a variety of efforts that make use of the sequencing data and capabilities of the JGI.

To understand the functional significance of DNA sequences, a JGI team led by a Livermore bioscientist compared human chromosome 19 with similar sections of mouse DNA. Their comparative analysis, published in *Science*, found that chromosome 19 had about 1,200 genes, substantiating earlier estimates that human DNA contains about 30,000 genes altogether. The team also discovered "candidate" regulatory sequences. Future research will test the function of these regulatory sequences to determine how and where they activate other genes.

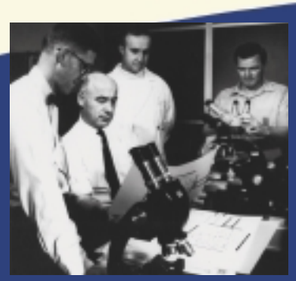
Efforts to sequence mouse DNA, which were carried out in 2000, made possible the comparative study. Sequencing work in 2001 also included studies of the Japanese pufferfish and parts of the *Yersinia pestis* genome. The pufferfish genome is of interest because it is compact yet similar to the human genome. In support of counter-bioterrorism, work on *Yersinia pestis*, the pathogen that causes plague, may lead to a better understanding of the organism's biology, better diagnostic tools, and new vaccines and treatments.

Laboratory scientists also developed a new DNA diagnostic technique that is expected to provide a valuable new tool to improve cancer diagnosis. The advance, described in *Proceedings of the National Academy of Sciences* in December 2001, allows researchers to detect mutations in individual cancer cells by specific identification and by making numerous copies of the DNA in the genes that are important for cancer progression in each cell.

1950s

The Atomic Energy Commission (AEC) began research on the possible biological consequences of fallout after the BRAVO test in 1954, which irradiated Marshall Islanders and Japanese fishermen. A growing need to understand the consequences of nuclear test activities led AEC to establish a limited program at the Laboratory in 1963.

1960s

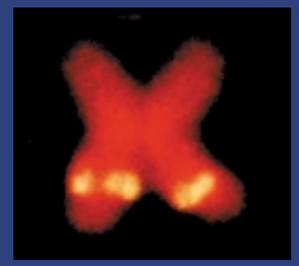


From its beginning, Livermore's biomedical program has focused on how ionizing radiation and chemicals affect genetic materials to understand health consequences. Researchers developed a computer-based system, CYDAC, to calculate the amount of DNA present in human chromosomes and check for abnormalities.

1970s

Chromosome biomarkers began to be used in studies of genetic damage, first with cultured animal cells. Taking a multidisciplinary approach to bioscience and using its expertise in lasers and engineering, the Laboratory developed tools such as a high-speed flow sorter for analyzing and purifying chromosomes and other molecules.

1980s



Tools such as the Laboratory's flow sorter led to chromosome painting in 1988, a much faster method of measuring damage to specific chromosomes. Chromosome research at the DOE laboratories attracted the attention of the National Academy of Sciences, which encouraged DOE's decision to launch the Human Genome Initiative in 1986.

1990s

Livermore's Human Genome Center completed a high-resolution map of chromosome 19 in 1996. Sequencing efforts expanded in 1999 with the opening of the tri-laboratory DOE Joint Genome Institute, which finished draft sequences of three chromosomes in 2000. The causes of several genetic diseases were identified through collaborative research.